Amendments to the Specification:

Please add the following paragraph following the title on page 1:

CROSS REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. Application No. 09/783,249, which claims the benefit to provisional application number 60/182,712, filed February 15, 2000.

Please rewrite the paragraph beginning on page 23, line 4 with the following paragraph:

R^{19} and R^{20} are each independently selected from the group: a bond to L_n, a bond to Q, hydrogen, $C_{1\text{-}10}$alkyl substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, ~~$C_{1\text{-}10}$cycloalkyl~~ $\underline{C_{3\text{-}10}\text{cycloalkyl}}$ substituted with 0-3 R^{23}, heterocyclo-$C_{1\text{-}10}$alkyl substituted with 0-3 R^{23}, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, $C_{6\text{-}10}$ aryl-$C_{1\text{-}10}$ alkyl substituted with 0-3 R^{23}, $C_{1\text{-}10}$alkyl-$C_{6\text{-}10}$aryl-substituted with 0-3 R^{23}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23}, and an electron, provided that when one of R^{19} or R^{20} is an electron, then the other is also an electron;

Please rewrite the paragraph beginning on page 35, line 21 with the following paragraph:

R^{19} and R^{20} are each independently selected from the group: a bond to the linking group, a bond to the targeting moiety, hydrogen, C_1-C_{10} alkyl substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, ~~$C_{1\text{-}10}$cycloalkyl~~ $\underline{C_{3\text{-}10}\text{cyclalkyl}}$ substituted with 0-3 R^{23}, heterocyclo-$C_{1\text{-}10}$alkyl substituted with 0-3 R^{23}, wherein the heterocyclo group is a

5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C_{6-10}aryl-C_{1-10}alkyl substituted with 0-3 R^{23}, C_{1-10}alkyl-C_{6-10}aryl-substituted with 0-3 R^{23}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23}, and an electron, provided that when one of R^{19} or R^{20} is an electron, then the other is also an electron;

Please rewrite the paragraph beginning on page 37, line 11 with the following paragraph:

(33) A diagnostic agent according to any one of ~~embodiments 1~~ **embodiments 1-32**, wherein:

x is 0;

Z is aryl substituted with 0-3 R^{16};

k is 1;

g' is 1;

R^{13a} R^{14a} are independently H;

W^2 is NHC(=O) or $-(OCH_2CH_2)_{76-84}$-; and

x' is 1.

Please rewrite the paragraph beginning on page 77, line 18 with the following paragraph:

Examples of heterocycles include, but are not limited to, 1H-indazole, 2-pyrrolidonyl, 2H,6H-1,5,2-dithiazinyl, 2H-pyrrolyl, 3H-indolyl, 4-piperidonyl, 4aH-carbazole, 4H-quinolizinyl, 6H-1,2,5-thiadiazinyl, acridinyl, azocinyl, benzimidazolyl, benzofuranyl, benzothiofuranyl, benzothiophenyl, benzoxazolyl, benzthiazolyl, benztriazolyl, benztetrazolyl, benzisoxazolyl, benzisothiazolyl, benzimidazalonyl, carbazolyl, 4a*H*-carbazolyl, ~~β-carbolinyl,~~ **β-carbolinyl,** chromanyl, chromenyl, cinnolinyl, decahydroquinolinyl, 2*H*,6*H*-1,5,2-dithiazinyl, dihydrofuro[2,3-*b*]tetrahydrofuran, furanyl, furazanyl, imidazolidinyl, imidazolinyl, imidazolyl, 1*H*-indazolyl, indolenyl, indolinyl,

indolizinyl, indolyl, isobenzofuranyl, isochromanyl, isoindazolyl, isoindolinyl, isoindolyl, isoquinolinyl, isothiazolyl, isoxazolyl, morpholinyl, naphthyridinyl, octahydroisoquinolinyl, oxadiazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, oxazolidinyl., oxazolyl, oxazolidinylperimidinyl, phenanthridinyl, phenanthrolinyl, phenarsazinyl, phenazinyl, phenothiazinyl, phenoxathiinyl, phenoxazinyl, phthalazinyl, piperazinyl, piperidinyl, pteridinyl, piperidonyl, 4-piperidonyl, pteridinyl, purinyl, pyranyl, pyrazinyl, pyrazolidinyl, pyrazolinyl, pyrazolyl, pyridazinyl, pyridooxazole, pyridoimidazole, pyridothiazole, pyridinyl, pyridyl, pyrimidinyl, pyrrolidinyl, pyrrolinyl, pyrrolyl, quinazolinyl, quinolinyl, 4*H*-quinolizinyl, quinoxalinyl, quinuclidinyl, carbolinyl, tetrahydrofuranyl, tetrahydroisoquinolinyl, tetrahydroquinolinyl, 6*H*-1,2,5-thiadiazinyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, thianthrenyl, thiazolyl, thienyl, thienothiazolyl, thienooxazolyl, thienoimidazolyl, thiophenyl, triazinyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl, xanthenyl. Preferred heterocycles include, but are not limited to, pyridinyl, furanyl, thienyl, pyrrolyl, pyrazolyl, imidazolyl, indolyl, benzimidazolyl, 1*H*-indazolyl, oxazolidinyl, benzotriazolyl, benzisoxazolyl, oxindolyl, benzoxazolinyl, or isatinoyl. Also included are fused ring and spiro compounds containing, for example, the above heterocycles.

Please rewrite the paragraph beginning on page 78, line 34 with the following paragraph:

A "cyclodextrin" is a cyclic oligosaccharide. Examples of cyclodextrins include, but are not limited to, ~~□-cyclodextrin, hydroxyethyl-□-cyclodextrin, hydroxypropyl-□-cyclodextrin, □-cyclodextrin, hydroxypropyl-□-cyclodextrin, carboxymethyl-□-cyclodextrin, dihydroxypropyl-□-cyclodextrin, hydroxyethyl-□-cyclodextrin, 2,6 di-O-methyl-□-cyclodextrin, sulfated-□-cyclodextrin, □-cyclodextrin, hydroxypropyl-□-cyclodextrin, dihydroxypropyl-□-cyclodextrin, hydroxyethyl-□-cyclodextrin, and sulfated-□-cyclodextrin~~

α-cyclodextrin, hydroxyethyl-α-cyclodextrin, hydroxypropyl-α-cyclodextrin, β-cyclodextrin, hydroxypropyl-β-cyclodextrin, carboxymethyl-β-cyclodextrin, dihydroxypropyl-β-cyclodextrin, hydroxyethyl-β-cyclodextrin, 2,6 di-O-methyl-

β-cyclodextrin, sulfated-β-cyclodextrin, γ-cyclodextrin, hydroxypropyl-γ -cyclodextrin, dihydroxypropyl-γ-cyclodextrin, hydroxyethyl-γ-cyclodextrin, and sulfated γ-cyclodextrin.

Please rewrite the paragraph beginning on page 139, line 26 with the following paragraph:

1. Initiate assay by adding 2 nM TACE to buffered solutions containing 10 ~~M~~ **μM** MCA peptide substrate in the presence of increasing concentrations of compound.

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims

Claims 1 to 103 ***(cancelled)***

104. ***(new)*** A method of detecting, imaging or monitoring congestive heart failure in a patient, comprising the steps of:

administering a diagnostic agent to the patient; and

acquiring an image of a site of concentration of the diagnostic agent in the patient by a diagnostic imaging technique;

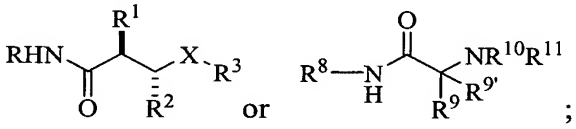
wherein the diagnostic agent comprises a diagnostic metal and a compound of the formula:

$$(Q)_d\text{-}(L_n)_x\text{-}K$$

or a pharmaceutically acceptable salt thereof;

wherein

Q is a matrix metalloproteinase inhibitor of formula (Ia) or (Ib):

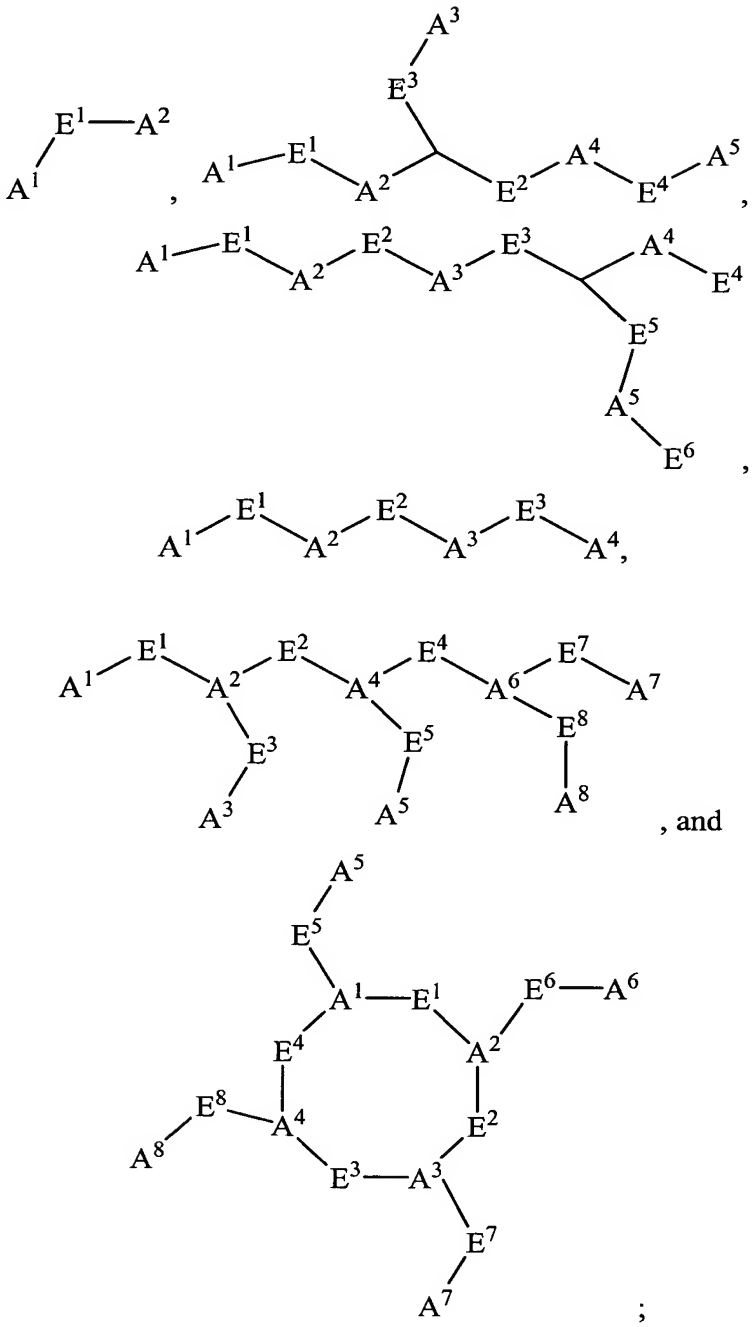


Ia or Ib ;

L_n is an optional linking group having the formula:

$$((W^1)_h\text{-}(CR^{13}R^{14})_g)_x\text{-}(Z)_k\text{-}((CR^{13a}R^{14a})_{g'}\text{-}(W^2)_{h'})_{x'};$$

K is a chelator having a formula selected from the group:



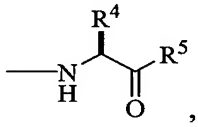
, and

;

R is independently OH or $-CH_2SH$;

R^1 is independently selected at each occurrence from the group: H, OH, C_{1-3}alkyl, C_{2-3}alkenyl, C_{2-3}alkynyl, and heterocycle-S-CH_2-;

R^2 is independently C_{1-20}alkyl;

X is independently C=O or SO_2, provided when X is C=O, R^3 is  , and when X is SO_2, R^3 is independently selected from the group: aryl substituted with 0-2 R^6, and heterocycle substituted with 0-2 R^6;

R^4 is independently selected at each occurrence from the group: C_{1-6}alkyl, phenyl, and benzyl;

R^5 is independently at each occurrence from the group: NH(C_{1-6}alkyl), NH-phenyl, and NH-heterocycle; wherein said alkyl, phenyl and heterocycle groups are optionally substituted with a bond to L_n or a bond to K;

R^6 is independently aryloxy substituted with 0-3 R^7;

R^7 is independently halogen or methoxy;

or alternatively,

R^1 and R^4 may be taken together to form a bridging group of the formula $-(CH_2)_3$-O-phenyl-CH_2-, optionally substituted with a bond to L_n or a bond to K;

or alternatively,

R^1 and R^2 may be taken together to form a bridging group of the formula $-(CH_2)_3$-NH-, optionally substituted with a bond to L_n or a bond to K; or

R^1 and R^2 taken together with the nitrogen and carbon atom through which they are attached form a saturated ring system containing 5-7 carbon atoms substituted with one or more substituents selected from the group consisting of: a bond to L_n, a bond to K, and $-C(=O)-NR^{29}R^{30}$;

R^8 is independently at each occurrence OH or phenyl, optionally substituted with a bond to L_n or a bond to K, provided that when R^8 is phenyl, R^{10} is $-C(=O)-CR^{12}$-NH-CH(CH_3)-COOH;

R^9 and $R^{9'}$ are independently H, C_{1-6}alkyl optionally substituted with a bond to L_n or a bond to K, or are taken together with the carbon atom to which R^9 and $R^{9'}$ are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system

containing 0-3 heteroatoms selected from O, N, SO_2 and S, said ring system substituted with R^6 and optionally substituted with a bond to L_n or a bond to K;

R^{10} and R^{11} are independently H, C_{1-6}alkyl optionally substituted with a bond to L_n or a bond to K, or are taken together with the nitrogen atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing, in addition to the nitrogen atom to which R^{10} and R^{11} are attached, 0-3 heteroatoms selected from O, N, SO_2 and S, said ring system optionally substituted with 0-3 R^{27}, a bond to L_n or a bond to K;

or alternatively,

R^9 and R^{10} are taken together with the carbon atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing, in addition to the nitrogen atom to which R^{10} is attached, 0-3 heteroatoms selected from O, N, SO_2 and S, said ring system optionally substituted with a bond to L_n or a bond to K;

R^{12} is independently C_{1-20}alkyl;

R^{27} is =O, C_{1-4}alkyl, or phenyl substituted with R^{28};

R^{28} is a phenoxy group substituted with 0-2 OCH_3 groups;

R^{29} and R^{30} taken together with the nitrogen atom through which they are attached form a saturated ring system containing 5-7 carbon atoms substituted with R^{31};

R^{31} is a benzyloxy group substituted with C_{1-4}alkyl;

d is selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

W^1 and W^2 are independently selected at each occurrence from the group: O, S, NH, NHC(=O), C(=O)NH, $NR^{15}C(=O)$, $C(=O)NR^{15}$, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO_2, SO_2NH, $-(OCH_2CH_2)_{76-84}$, $(OCH_2CH_2)_s$, $(CH_2CH_2O)_{s'}$, $(OCH_2CH_2CH_2)_{s''}$, $(CH_2CH_2CH_2O)_t$, and $(aa)_{t'}$;

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-3 R^{16}, C_{3-10}cycloalkyl substituted with 0-3 R^{16}, and a 5-10 membered heterocyclic ring system containing

1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{16};

R^{13}, R^{13a}, R^{14}, R^{14a}, and R^{15} are independently selected at each occurrence from the group: H, =O, COOH, SO_3H, PO_3H, C_{1-5}alkyl substituted with 0-3 R^{16}, aryl substituted with 0-3 R^{16}, benzyl substituted with 0-3 R^{16}, and C_{1-5}alkoxy substituted with 0-3 R^{16}, $NHC(=O)R^{17}$, $C(=O)NHR^{17}$, $NHC(=O)NHR^{17}$, NHR^{17}, R^{17}, and a bond to K;

R^{16} is independently selected at each occurrence from the group: a bond to K, $COOR^{17}$, $C(=O)NHR^{17}$, $NHC(=O)R^{17}$, OH, NHR^{17}, SO_3H, PO_3H, $-OPO_3H_2$, $-OSO_3H$, aryl substituted with 0-3 R^{17}, C_{1-5}alkyl substituted with 0-1 R^{18}, C_{1-5}alkoxy substituted with 0-1 R^{18}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{17};

R^{17} is independently selected at each occurrence from the group: H, alkyl substituted with 0-1 R^{18}, aryl substituted with 0-1 R^{18}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R^{18}, C_{3-10}cycloalkyl substituted with 0-1 R^{18}, polyalkylene glycol substituted with 0-1 R^{18}, carbohydrate substituted with 0-1 R^{18}, cyclodextrin substituted with 0-1 R^{18}, amino acid substituted with 0-1 R^{18}, polycarboxyalkyl substituted with 0-1 R^{18}, polyazaalkyl substituted with 0-1 R^{18}, peptide substituted with 0-1 R^{18}, wherein the peptide is comprised of 2-10 amino acids, 3,6-O-disulfo-B-D-galactopyranosyl, bis(phosphonomethyl)glycine, and a bond to K;

R^{18} is a bond to K;

k is selected from 0, 1, and 2;

h is selected from 0, 1, and 2;

h' is selected from 0, 1, and 2;

g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s" is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

t is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

x is selected from 0, 1, 2, 3, 4, and 5;

x' is selected from 0, 1, 2, 3, 4, and 5;

x" is selected from 0 and 1;

A^1, A^2, A^3, A^4, A^5, A^6, A^7, and A^8 are independently selected at each occurrence from the group: N, NR^{26}, NR^{19}, $NR^{19}R^{20}$, S, SH, –S(Pg), O, OH, PR^{19}, $PR^{19}R^{20}$, -O-P(O)(R^{21})-O-, $P(O)R^{21}R^{22}$, a bond to Q and a bond to L_n;

Pg is a thiol protecting group;

E^1, E^2, E^3, E^4, E^5, E^6, E^7, and E^8 are independently a bond, CH, or a spacer group independently selected at each occurrence from the group: $C_{1\text{-}16}$alkyl substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, $C_{3\text{-}10}$cycloalkyl substituted with 0-3 R^{23}, heterocyclo-$C_{1\text{-}10}$alkyl substituted with 0-3 R^{23}, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, $C_{6\text{-}10}$aryl-$C_{1\text{-}10}$alkyl substituted with 0-3 R^{23}, $C_{1\text{-}10}$alkyl-$C_{6\text{-}10}$aryl-substituted with 0-3 R^{23}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23};

R^{19} and R^{20} are each independently selected from the group: a bond to L_n, a bond to Q, hydrogen, $C_{1\text{-}10}$alkyl substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, $C_{3\text{-}10}$cycloalkyl substituted with 0-3 R^{23}, heterocyclo-$C_{1\text{-}10}$alkyl substituted with 0-3 R^{23}, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, $C_{6\text{-}10}$ aryl-$C_{1\text{-}10}$ alkyl substituted with 0-3 R^{23}, $C_{1\text{-}10}$alkyl-$C_{6\text{-}10}$aryl-substituted with 0-3 R^{23}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently

selected from N, S, and O and substituted with 0-3 R^{23}, and an electron, provided that when one of R^{19} or R^{20} is an electron, then the other is also an electron;

R^{21} and R^{22} are each independently selected from the group: a bond to L_n, a bond to Q, -OH, C_{1-10}alkyl substituted with 0-3 R^{23}, C_{1-10}alkyl substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, C_{3-10}cycloalkyl substituted with 0-3 R^{23}, heterocyclo-C_{1-10}alkyl substituted with 0-3 R^{23}, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C_{6-10}aryl-C_{1-10}alkyl substituted with 0-3 R^{23}, C_{1-10}alkyl-C_{6-10}aryl-substituted with 0-3 R^{23}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23};

R^{23} is independently selected at each occurrence from the group: a bond to L_n, a bond to Q, =O, F, Cl, Br, I, $-CF_3$, -CN, $-CO_2R^{24}$, $-C(=O)R^{24}$, $-C(=O)N(R^{24})_2$, -CHO, $-CH_2OR^{24}$, $-OC(=O)R^{24}$, $-OC(=O)OR^{24a}$, $-OR^{24}$, $-OC(=O)N(R^{24})_2$, $-NR^{25}C(=O)R^{24}$, $-NR^{25}C(=O)OR^{24a}$, $-NR^{25}C(=O)N(R^{24})_2$, $-NR^{25}SO_2N(R^{24})_2$, $-NR^{25}SO_2R^{24a}$, $-SO_3H$, $-SO_2R^{24a}$, $-SR^{24}$, $-S(=O)R^{24a}$, $-SO_2N(R^{24})_2$, $-N(R^{24})_2$, $-NHC(=S)NHR^{24}$, $=NOR^{24}$, NO_2, $-C(=O)NHOR^{24}$, $-C(=O)NHNR^{24}R^{24a}$, $-OCH_2CO_2H$, 2-(1-morpholino)ethoxy, C_{1-5}alkyl, C_{2-4}alkenyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkylmethyl, C_{2-6}alkoxyalkyl, aryl substituted with 0-2 R^{24}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O;

wherein at least one of A^1, A^2, A^3, A^4, A^5, A^6, A^7, A^8 or R^{23} is a bond to L_n or Q;

R^{24}, R^{24a}, and R^{25} are independently selected at each occurrence from the group: a bond to L_n, a bond to Q, H, C_{1-6}alkyl, phenyl, benzyl, C_{1-6}alkoxy, halide, nitro, cyano, and trifluoromethyl; and

R^{26} is a co-ordinate bond to a metal or a hydrazine protecting group; or

a pharmaceutically acceptable salt thereof.

105. ***(new)*** A method according to claim 104, wherein:

R is OH;

R^1 is independently selected at each occurrence from the group: H, OH, C_{1-3}alkyl, C_{2-3}alkenyl, C_{2-3}alkynyl, and heterocycle-S-CH_2-;

R^2 is independently C_{1-6}alkyl;

X is C=O;

R^4 is independently selected at each occurrence from the group: C_{1-6}alkyl, phenyl, and benzyl;

R^8 is OH;

R^9 and $R^{9'}$ are independently H, C_{1-6}alkyl optionally substituted with a bond to L_n or a bond to K, or are taken together with the carbon atom to which R^9 and $R^{9'}$ are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-1 heteroatoms selected from O, N, SO_2 and S, said ring system optionally substituted with a bond to L_n or a bond to K;

R^{10} and R^{11} are independently H, or C_{1-6}alkyl optionally substituted with a bond to L_n or a bond to K, or are taken together with the nitrogen atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing, in addition to the nitrogen atom to which R^{10} and R^{11} are attached, 0-1 heteroatoms selected from O, N, SO_2 and S, said ring system optionally substituted with 0-3 R^{27}, a bond to L_n or a bond to K;

or alternatively,

R^9 and R^{10} are taken together with the carbon atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing, in addition to the nitrogen atom to which R^{10} is attached, 0-1 heteroatoms selected from O, N, SO_2, and S, said ring system optionally substituted with a bond to L_n or a bond to K; and

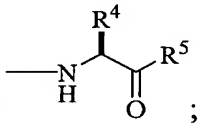
R^{12} is independently C_{1-6}alkyl.

106. ***(new)*** A method according to claim 104, wherein:

R is –OH;

R^2 is $C_{1\text{-}6}$alkyl;

X is C=O;

R^3 is  ;

R^1 and R^4 are taken together to form a bridging group of formula $-(CH_2)_3$-O-phenyl-CH_2-; and

R^5 is NH($C_{1\text{-}6}$alkyl), substituted with a bond to L_n or a bond to K.

107. ***(new)*** A method according to claim 104, wherein:

R is –OH;

R^9 is C_1alkyl substituted with a bond to L_n; and

R^{10} and R^{11} taken together with the nitrogen atom to which they are attached form a 5 atom saturated ring system, said ring system substituted with 0-3 R^{27}.

108. ***(new)*** A method according to claim 104, wherein:

R is –OH; and

R^1 and R^2 taken together with the nitrogen and carbon atom through which they are attached form a saturated ring system containing 5-7 carbon atoms substituted with one or more substituents selected from the group consisting of: a bond to L_n, a bond to K, and $-C(=O)-NR^{29}R^{30}$.

109. ***(new)*** A method according to claim 104, wherein:

Z is selected from the group: aryl substituted with 0-1 R^{16}, $C_{3\text{-}10}$ cycloalkyl substituted with 0-1 R^{16}, and a 5-10 membered heterocyclic ring system containing

1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R^{16};

R^{13}, R^{13a}, R^{14}, R^{14a}, and R^{15} are independently selected at each occurrence from the group: H, =O, COOH, SO_3H, $C_{1\text{-}5}$alkyl substituted with 0-1 R^{16}, aryl substituted with 0-1 R^{16}, benzyl substituted with 0-1 R^{16}, and $C_{1\text{-}5}$alkoxy substituted with 0-1 R^{16}, $NHC(=O)R^{17}$, $C(=O)NHR^{17}$, $NHC(=O)NHR^{17}$, NHR^{17}, R^{17}, and a bond to K;

k is 0 or 1;

s is selected from 0, 1, 2, 3, 4, and 5;

s' is selected from 0, 1, 2, 3, 4, and 5;

s" is selected from 0, 1, 2, 3, 4, and 5; and

t is selected from 0, 1, 2, 3, 4, and 5.

110. ***(new)*** A method according to claim 104, wherein:

W^1 is $C(=O)NR^{15}$;

h is 1;

g is 3;

R^{13} and R^{14} are independently H;

x is 1;

k is 0;

g' is 0;

h' is 1;

W^2 is NH; and

x' is 1.

111. ***(new)*** A method according to claim 104, wherein:

x is 0;

k is 1;

Z is aryl substituted with 0-3 R^{16};

g' is 1;

W^2 is NH;

R^{13a} and R^{14a} are independently H;

h' is 1; and

x' is 1.

112. ***(new)*** A method according to claim 104, wherein:

W^1 is $C(=O)NR^{15}$;

h is 1;

g is 2;

R^{13} and R^{14} are independently H;

x is 1;

k is 0;

g' is 1;

R^{13a} and R^{14a} are independently H; or C_{1-5}alkyl substituted with 0-3 R^{16};

R^{16} is SO_3H;

W^2 is NHC(=O) or NH;

h' is 1; and

x' is 2.

113. ***(new)*** A method according to claim 104, wherein:

W^1 is C(=O)NH;

h is 1;

g is 3;

R^{13} and R^{14} are independently H;

k is 0;

g' is 0;

x is 1;

W^2 is -NH(C=O)- or $-(OCH_2CH_2)_{76-84}$-;

h' is 2; and

x' is 1.

114. ***(new)*** A method according to claim 104, wherein:

x is 0;

k is 0;

g' is 3;

h' is 1;

W^2 is NH; and

x' is 1.

115. ***(new)*** A method according to claim 104, wherein

x is 0;

Z is aryl substituted with 0-3 R^{16};

k is 1;

g' is 1;

R^{13a} and R^{14a} are independently H;

W^2 is NHC(=O) or $-(OCH_2CH_2)_{76\text{-}84}$-; and

x' is 1.

116. ***(new)*** A method according to claim 104, wherein:

W^1 is C=O;

g is 2;

R^{13} and R^{14} are independently H;

k is 0;

g' is 0;

h' is 1;

W^2 is NH; and

x' is 1.

117. ***(new)*** A method according to claim 104, wherein:

h' is 1;

W^2 is NH; and

x' is 1.

118. ***(new)*** A method according to claim 104, wherein:

x is 0;

Z is aryl substituted with 0-3 R^{16};

k is 1;

g' is 1;

R^{13a} and R^{14a} are independently H;

W^2 is NHC(=O) or $-(OCH_2CH_2)_{76-84}$-; and

x' is 1.

119. ***(new)*** A method according to claim 104, wherein:

W^1 is C=O;

g is 2;

R^{13} and R^{14} are independently H;

k is 0;

g' is 0;

h' is 1;

W^2 is NH; and

x' is 1.

120. ***(new)*** A method according to claim 104, wherein

A^1, A^2, A^3, A^4, A^5, A^6, A^7, and A^8 are independently selected at each occurrence from the group: NR^{19}, $NR^{19}R^{20}$, S, SH, OH, a bond to Q and a bond to L_n;

E^1, E^2, E^3, E^4, E^5, E^6, E^7, and E^8 are independently a bond, CH, or a spacer group independently selected at each occurrence from the group: C_{1-10}alkyl substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, C_{3-10}cycloalkyl substituted with

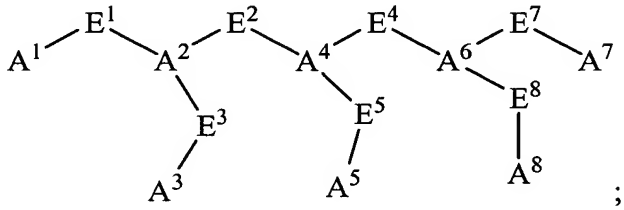
0-3 R^{23}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23};

R^{19} and R^{20} are each independently selected from the group: a bond to Q, a bond to L_n, hydrogen, C_{1-10}alkyl substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23}, and an electron;

R^{23} is independently selected at each occurrence from the group: a bond to Q, a bond to L_n, =O, F, Cl, Br, I, $-CF_3$, -CN, $-CO_2R^{24}$, $-C(=O)R^{24}$, $-C(=O)N(R^{24})_2$, $-CH_2OR^{24}$, $-OC(=O)R^{24}$, $-OC(=O)OR^{24a}$, $-OR^{24}$, $-OC(=O)N(R^{24})_2$, $-NR^{25}C(=O)R^{24}$, $-NR^{25}C(=O)OR^{24a}$, $-NR^{25}C(=O)N(R^{24})_2$, $-NR^{25}SO_2N(R^{24})_2$, $-NR^{25}SO_2R^{24a}$, $-SO_3H$, $-SO_2R^{24a}$, $-S(=O)R^{24a}$, $-SO_2N(R^{24})_2$, $-N(R^{24})_2$, $-NHC(=S)NHR^{24}$, $=NOR^{24}$, $-C(=O)NHNR^{24}R^{24a}$, $-OCH_2CO_2H$, and 2-(1-morpholino)ethoxy; and

R^{24}, R^{24a}, and R^{25} are independently selected at each occurrence from the group: a bond to L_n, H, and C_{1-6}alkyl.

121. ***(new)*** A method according to claim 104, wherein K is:



;

A^1 is a bond to L_n;

A^2, A^4, and A^6 are each N;

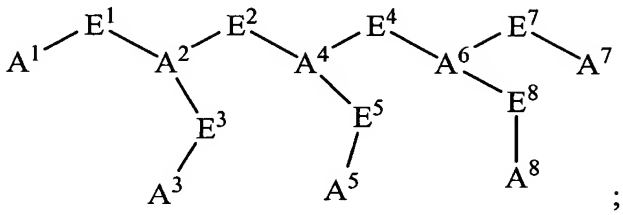
A^3, A^5, A^7 and A^8 are each OH;

E^1, E^2, and E^4 are C_2alkyl;

E^3, E^5, E^7, and E^8 are C_2alkyl substituted with 0-1 R^{23}; and

R^{23} is =O.

122. ***(new)*** A method according to claim 104, wherein K is:



;

wherein:

A^5 is a bond to Ln;

A^1, A^3, A^7 and A^8 are each OH;

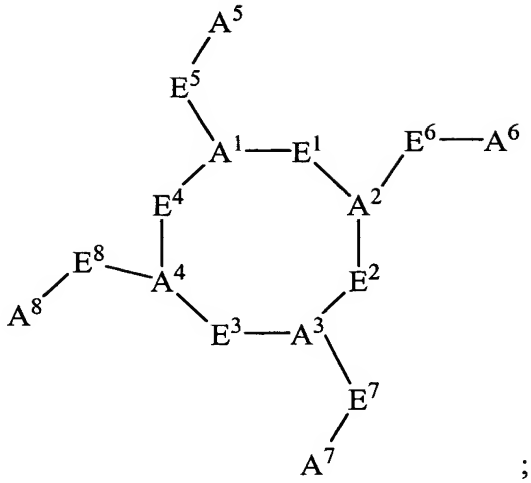
A^2, A^4 and A^6 are each N;

E^1, E^3, E^5, E^7, and E^8 are C_2 alkyl substituted with 0-1 R^{23};

E^2 and E^4 are C_2 alkyl; and

R^{23} is =O.

123. ***(new)*** A method according to claim 104, wherein K is:



;

A^1, A^2, A^3 and A^4 are each N;

A^5, A^6 and A^8 are each OH;

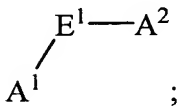
A^7 is a bond to L_n;

E^1, E^2, E^3, E^4 are each independently C_2alkyl; and

E^5, E^6, E^7, E^8 are each independently C_2alkyl substituted with 0-1 R^{23}; and

R^{23} is =O.

124. ***(new)*** A method according to claim 104, wherein K is:



;

A^1 is NR^{26};

R^{26} is a co-ordinate bond to a metal or a hydrazine protecting group;

E^1 is a bond;

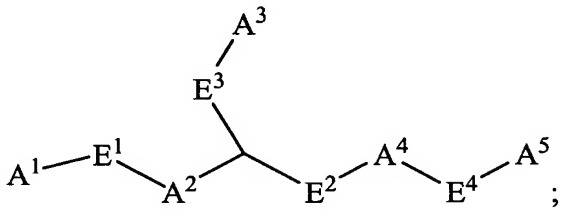
A^2 is NHR^{19};

R^{19} is a heterocycle substituted with R^{23}, the heterocycle being selected from pyridine and pyrimidine;

R^{23} is selected from a bond to L_n, $C(=O)NHR^{24}$ and $C(=O)R^{24}$; and

R^{24} is a bond to L_n.

125. ***(new)*** A method according to claim 104, wherein wherein K is:



wherein:

A^1 and A^5 are each –S(Pg);

E^1 and E^4 are C_2alkyl substituted with 0-1 R^{23};

R^{23} is =O;

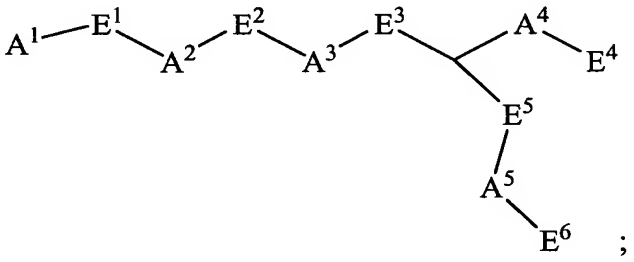
A^2 and A^4 are each –NH;

E^2 is CH_2;

E^3 is C_{1-3} alkyl substituted with 0-1 R^{23}; and

A^3 is a bond to Ln.

126. ***(new)*** A method according to claim 104, wherein K is:



wherein:

A^1 is a bond to Ln;

E^1 is C_1alkyl substituted by R^{23};

A^2 is NH;

E^2 is C_2alkyl substituted with 0-1 R^{23};

A^3 is –O-P(O)(R^{21})-O-;

E^3 is C_1alkyl;

A^4 and A^5 are each –O-;

E^4 and E^6 are each independently $C_{1\text{-}16}$alkyl substituted with 0-1R^{23};

E^5 is C_1 alkyl;

R^{21} is –OH; and

R^{23} is =O.

127. ***(new)*** A method according to claim 104, wherein the compound is:

2-{[5-(3-{2-[(6-Hydroxycarbamoyl-7-isobutyl-8-oxo-2-oxa-9-aza-bicyclo[10.2.2]hexadeca-1(15),12(16),13-triene-10-carbonyl)-amino]-acetylamino}-propylcarbamoyl)-pyridin-2-yl]-hydrazonomethyl}-benzenesulfonic acid;

2-{[5-(4-{[(6-Hydroxycarbamoyl-7-isobutyl-8-oxo-2-oxa-9-aza-bicyclo[10.2.2]hexadeca-1(15),12(16),13-triene-10-carbonyl)-amino]-methyl}-benzylcarbamoyl)-pyridin-2-yl]-hydrazonomethyl}-benzenesulfonic acid;

2-[7-({N-[3-(2-{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino}acetylamino)propyl]carbamoyl}methyl)-1,4,7,10-tetraaza-4,10-bis(carboxymethyl)cyclododecyl]acetic acid;

2-{7-[(N-{[4-({[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]-carbonylamino}methyl)phenyl]methyl}carbamoyl)methyl]-1,4,7,10-tetraaza-4,10-bis(carboxymethyl)cyclododecyl}acetic acid;

2-(7-{[N-(1-{N-[3-(2-{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino}acetylamino)propyl]carbamoyl}-2-sulfoethyl)carbamoyl]methyl}-1,4,7,10-tetraaza-4,10-bis(carboxymethyl)cyclododecyl)acetic acid;

2-[7-({N-[1-(N-{[4-({[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]-

carbonylamino}methyl)phenyl]methyl}carbamoyl)-2-sulfoethyl]carbamoyl}methyl)-1,4,7,10-tetraaza-4,10-bis(carboxymethyl)cyclododecyl]acetic acid;

2-({2-[({N-[3-(2-{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino}acetylamino)propyl]carbamoyl}methyl)(carboxymethyl)amino}ethyl){2-[bis(carboxymethyl)amino]ethyl}amino]acetic acid;

2-[(2-{[(N-{[4-({[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]-carbonylamino}methyl)phenyl]methyl}carbamoyl)methyl](carboxymethyl)amino}ethyl){2-[bis(carboxymethyl)amino]ethyl}amino]acetic acid;

N-[3-(2-{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino}acetylamino)propyl]-4,5-bis[2-(ethoxyethylthio)acetylamino]pentanamide;

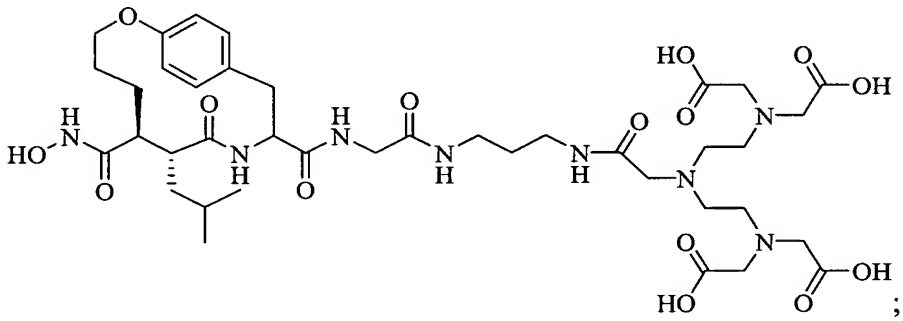
N-{[4-({[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino}methyl)-phenyl]methyl}-4,5-bis[2-(ethoxyethylthio)acetylamino]-pentanamide;

1-(1,2-Dipalmitoyl-sn-glycero-3-phosphoethanolamino)-α,ω-dicarbonylPEG3400-2-{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino}-N-(3-aminopropyl)acetamide;

1-(1,2-Dipalmitoyl-sn-glycero-3-phosphoethanolamino)-α,ω-dicarbonylPEG3400-[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]-N-{[4-(aminomethyl)phenyl]methyl}carboxamide conjugate;

2-[2-({5-[N-(5-(N-hydroxycarbamoyl)(5R)-5-{3-[4-(3,4-dimethoxyphenoxy)phenyl]-3-methyl-2-oxopyrrolidinyl}pentyl)carbamoyl](2-pyridyl)}amino)(1Z)-2-azavinyl]benzenesulfonic acid;

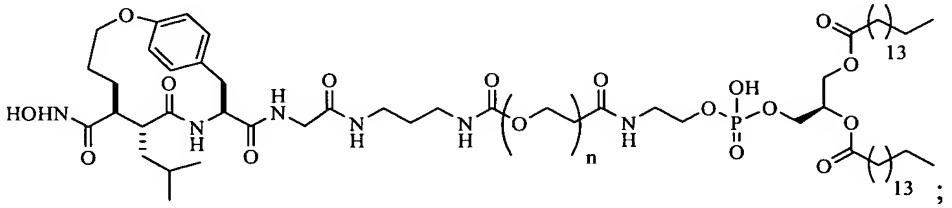
2-(2-{[5-(N-{3-[3-(N-hydroxycarbamoyl)(4S)-4-({4-[(4-methylphenyl)methoxy]piperidyl}carbonyl)piperidyl]-3-oxopropyl}carbamoyl)(2-pyridyl)]amino}(1Z)-2-azavinyl)benzenesulfonic acid;



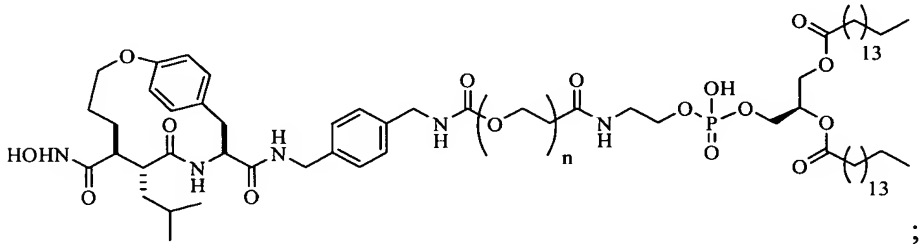
; or

a pharmaceutically acceptable salt thereof.

128. ***(new)*** A method according to claim 104, wherein the compound is:



;



; or

pharmaceutically acceptable salt thereof.

129. ***(new)*** A method according to claim 104, wherein the diagnostic metal is selected from the group consisting of: a paramagnetic metal, a ferromagnetic metal, a gamma-emitting radioisotope, positron-emitting radioisotope and an x-ray absorber.

130. ***(new)*** A method according to claim 129, wherein the diagnostic metal is a gamma-emitting radioisotope selected from the group consisting of ^{99m}Tc, ^{95}Tc, ^{111}In, ^{62}Cu, ^{64}Cu, ^{67}Ga, and ^{68}Ga.

131. ***(new)*** A method according to claim 130, further comprising a first ancillary ligand and a second ancillary ligand capable of stabilizing the gamma-emitting radioisotope.

132. ***(new)*** A method according to claim 130, wherein the gamma-emitting radioisotope is ^{99}mTc.

133. ***(new)*** A method according to claim 130, wherein the gamma-emitting radioisotope is ^{111}In.

134. ***(new)*** A method according to claim 129, wherein the paramagnetic metal ion is selected from the group consisting of Gd(III), Dy(III), Fe(III), and Mn(II).

135. ***(new)*** A method according to claim 129, wherein the x-ray absorber is a metal is selected from the group consisting of: Re, Sm, Ho, Lu, Pm, Y, Bi, Pd, Gd, La, Au, Au, Yb, Dy, Cu, Rh, Ag, and Ir.

136. ***(new)*** A method of detecting, imaging or monitoring congestive heart failure in a patient, comprising the steps of:

administering a diagnostic agent to the patient; and

acquiring an image of a site of concentration of the diagnostic agent in the patient by a diagnostic imaging technique;

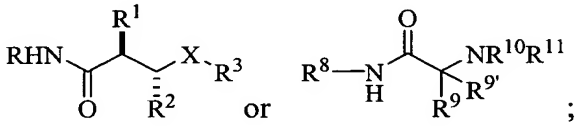
wherein the diagnostic agent comprises an echogenic gas and a compound of the formula:

$$(Q)_d\text{-}(L_n)_x\text{-}K$$

or a pharmaceutically acceptable salt thereof;

wherein

Q is a matrix metalloproteinase inhibitor of formula (Ia) or (Ib):

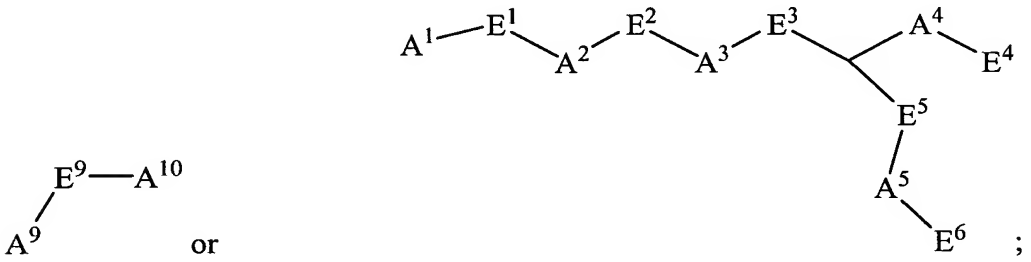


Ia Ib

L_n is an optional linking group having the formula:

$$((W^1)_h\text{-}(CR^{13}R^{14})_g)_x\text{-}(Z)_k\text{-}((CR^{13a}R^{14a})_{g'}\text{-}(W^2)_{h'})_{x'};$$

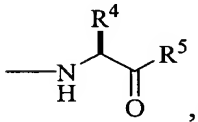
K is a surfactant capable of forming an echogenic gas filled lipid sphere or microbubble, wherein the surfactant is a lipid or a compound having a formula selected from the group:



R is independently OH or $-CH_2SH$;

R^1 is independently selected at each occurrence from the group: H, OH, $C_{1\text{-}3}$alkyl, $C_{2\text{-}3}$alkenyl, $C_{2\text{-}3}$alkynyl, and heterocycle-S-CH_2-;

R^2 is independently $C_{1\text{-}20}$alkyl;

X is independently C=O or SO_2, provided when X is C=O, R^3 is  , and when X is SO_2, R^3 is independently selected from the group: aryl substituted with 0-2 R^6, and heterocycle substituted with 0-2 R^6;

R^4 is independently selected at each occurrence from the group: $C_{1\text{-}6}$alkyl, phenyl, and benzyl;

R^5 is independently at each occurrence from the group: NH(C_{1-6}alkyl), NH-phenyl, and NH-heterocycle; wherein said alkyl, phenyl and heterocycle groups are optionally substituted with a bond to L_n or a bond to K;

R^6 is independently aryloxy substituted with 0-3 R^7;

R^7 is independently halogen or methoxy;

or alternatively,

R^1 and R^4 may be taken together to form a bridging group of the formula $-(CH_2)_3$-O-phenyl-CH_2-, optionally substituted with a bond to L_n or a bond to K;

or alternatively,

R^1 and R^2 may be taken together to form a bridging group of the formula $-(CH_2)_3$-NH-, optionally substituted with a bond to L_n or a bond to K; or

R^1 and R^2 taken together with the nitrogen and carbon atom through which they are attached form a saturated ring system containing 5-7 carbon atoms substituted with one or more substituents selected from the group consisting of: a bond to L_n, a bond to K, and $-C(=O)-NR^{29}R^{30}$;

R^8 is independently at each occurrence OH or phenyl, optionally substituted with a bond to L_n or a bond to K, provided that when R^8 is phenyl, R^{10} is $-C(=O)-CR^{12}$-NH-$CH(CH_3)$-COOH;

R^9 and $R^{9'}$ are independently H, C_{1-6}alkyl optionally substituted with a bond to L_n or a bond to K, or are taken together with the carbon atom to which R^9 and $R^{9'}$ are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO_2 and S, said ring system substituted with R^6 and optionally substituted with a bond to L_n or a bond to K;

R^{10} and R^{11} are independently H, or C_{1-6}alkyl optionally substituted with a bond to L_n or a bond to K, or are taken together with the nitrogen atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing, in addition to the nitrogen atom to which R^{10} and R^{11} are attached, 0-3 heteroatoms selected from O, N, SO_2 and S, said ring system optionally substituted with 0-3 R^{27}, a bond to L_n or a bond to K;

or alternatively,

R^9 and R^{10} are taken together with the carbon atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing, in addition to the nitrogen atom to which R^{10} is attached, 0-3 heteroatoms selected from O, N, SO_2 and S, said ring system optionally substituted with a bond to L_n or a bond to K;

R^{12} is independently C_{1-20}alkyl;

R^{27} is =O, C_{1-4}alkyl, or phenyl substituted with R^{28};

R^{28} is a phenoxy group substituted with 0-2 OCH_3 groups;

R^{29} and R^{30} taken together with the nitrogen atom through which they are attached form a saturated ring system containing 5-7 carbon atoms substituted with R^{31};

R^{31} is a benzyloxy group substituted with C_{1-4}alkyl;

d is selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

W^1 and W^2 are independently selected at each occurrence from the group: O, S, NH, NHC(=O), C(=O)NH, $NR^{15}C(=O)$, $C(=O)NR^{15}$, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO_2, SO_2NH, $-(OCH_2CH_2)_{76-84}$, $(OCH_2CH_2)_s$, $(CH_2CH_2O)_{s'}$, $(OCH_2CH_2CH_2)_{s''}$, $(CH_2CH_2CH_2O)_t$, and $(aa)_{t'}$;

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-3 R^{16}, C_{3-10}cycloalkyl substituted with 0-3 R^{16}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{16};

R^{13}, R^{13a}, R^{14}, R^{14a}, and R^{15} are independently selected at each occurrence from the group: H, =O, COOH, SO_3H, PO_3H, C_{1-5}alkyl substituted with 0-3 R^{16}, aryl substituted with 0-3 R^{16}, benzyl substituted with 0-3 R^{16}, and C_{1-5}alkoxy substituted with 0-3 R^{16}, $NHC(=O)R^{17}$, $C(=O)NHR^{17}$, $NHC(=O)NHR^{17}$, NHR^{17}, R^{17}, and a bond to K;

R^{16} is independently selected at each occurrence from the group: a bond to K, $COOR^{17}$, $C(=O)NHR^{17}$, $NHC(=O)R^{17}$, OH, NHR^{17}, SO_3H, PO_3H, $-OPO_3H_2$, $-OSO_3H$, aryl substituted with 0-3 R^{17}, C_{1-5}alkyl substituted with 0-1 R^{18}, C_{1-5}alkoxy substituted with 0-1 R^{18}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{17};

R^{17} is independently selected at each occurrence from the group: H, alkyl substituted with 0-1 R^{18}, aryl substituted with 0-1 R^{18}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R^{18}, C_{3-10}cycloalkyl substituted with 0-1 R^{18}, polyalkylene glycol substituted with 0-1 R^{18}, carbohydrate substituted with 0-1 R^{18}, cyclodextrin substituted with 0-1 R^{18}, amino acid substituted with 0-1 R^{18}, polycarboxyalkyl substituted with 0-1 R^{18}, polyazaalkyl substituted with 0-1 R^{18}, peptide substituted with 0-1 R^{18}, wherein the peptide is comprised of 2-10 amino acids, 3,6-O-disulfo-B-D-galactopyranosyl, bis(phosphonomethyl)glycine, and a bond to K;

R^{18} is a bond to K;

k is selected from 0, 1, and 2;

h is selected from 0, 1, and 2;

h' is selected from 0, 1, and 2;

g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s" is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

t is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

x is selected from 0, 1, 2, 3, 4, and 5;

x' is selected from 0, 1, 2, 3, 4, and 5;

x" is selected from 0 and 1;

A^1, A^2, A^3, A^4, A^5, and A^6 are independently selected at each occurrence from the group: N, NR^{26},NR^{19}, $NR^{19}R^{20}$, S, SH, –S(Pg), O, OH, PR^{19}, $PR^{19}R^{20}$, -O-P(O)(R^{21})-O-, P(O)$R^{21}R^{22}$, a bond to Q and a bond to L_n;

A^9 is selected from the group: OH and OR^{32};

A^{10} is OR^{32};

R^{32} is $C(=O)C_{1\text{-}20}$alkyl;

Pg is a thiol protecting group;

E^1, E^2, E^3, E^4, and E^5 are independently a bond, CH, or a spacer group independently selected at each occurrence from the group: $C_{1\text{-}16}$alkyl substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, $C_{3\text{-}10}$cycloalkyl substituted with 0-3 R^{23}, heterocyclo-$C_{1\text{-}10}$alkyl substituted with 0-3 R^{23}, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, $C_{6\text{-}10}$aryl-$C_{1\text{-}10}$alkyl substituted with 0-3 R^{23}, $C_{1\text{-}10}$alkyl-$C_{6\text{-}10}$aryl-substituted with 0-3 R^{23}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23};

E^9 is $C_{1\text{-}10}$alkylene substituted with 1-3 R^{33};

R^{33} is independently selected at each occurrence from the group: R^{35}, -PO_3H-R^{35}, =O, -CO_2R^{34}, -C(=O)R^{34}, -C(=O)N(R^{34})$_2$, -CH_2OR^{34}, -OR^{34}, -N(R^{34})$_2$, $C_{1\text{-}5}$alkyl, and $C_{2\text{-}4}$alkenyl;

R^{34} is independently selected at each occurrence from the group: R^{35}, H, $C_{1\text{-}6}$alkyl, phenyl, benzyl, and trifluoromethyl;

R^{35} is a bond to L_n;

R^{19} and R^{20} are each independently selected from the group: a bond to L_n, a bond to Q, hydrogen, $C_{1\text{-}10}$alkyl substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, $C_{3\text{-}10}$cycloalkyl substituted with 0-3 R^{23}, heterocyclo-$C_{1\text{-}10}$alkyl substituted with 0-3 R^{23}, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system

containing 1-4 heteroatoms independently selected from N, S, and O, C_{6-10} aryl-C_{1-10} alkyl substituted with 0-3 R^{23}, C_{1-10}alkyl-C_{6-10}aryl-substituted with 0-3 R^{23}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23}, and an electron, provided that when one of R^{19} or R^{20} is an electron, then the other is also an electron;

R^{21} and R^{22} are each independently selected from the group: a bond to L_n, a bond to Q, -OH, C_{1-10}alkyl substituted with 0-3 R^{23}, C_{1-10}alkyl substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, C_{3-10}cycloalkyl substituted with 0-3 R^{23}, heterocyclo-C_{1-10}alkyl substituted with 0-3 R^{23}, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C_{6-10}aryl-C_{1-10}alkyl substituted with 0-3 R^{23}, C_{1-10}alkyl-C_{6-10}aryl-substituted with 0-3 R^{23}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23};

R^{23} is independently selected at each occurrence from the group: a bond to L_n, a bond to Q, =O, F, Cl, Br, I, $-CF_3$, -CN, $-CO_2R^{24}$, $-C(=O)R^{24}$, $-C(=O)N(R^{24})_2$, -CHO, $-CH_2OR^{24}$, $-OC(=O)R^{24}$, $-OC(=O)OR^{24a}$, $-OR^{24}$, $-OC(=O)N(R^{24})_2$, $-NR^{25}C(=O)R^{24}$, $-NR^{25}C(=O)OR^{24a}$, $-NR^{25}C(=O)N(R^{24})_2$, $-NR^{25}SO_2N(R^{24})_2$, $-NR^{25}SO_2R^{24a}$, $-SO_3H$, $-SO_2R^{24a}$, $-SR^{24}$, $-S(=O)R^{24a}$, $-SO_2N(R^{24})_2$, $-N(R^{24})_2$, $-NHC(=S)NHR^{24}$, $=NOR^{24}$, NO_2, $-C(=O)NHOR^{24}$, $-C(=O)NHNR^{24}R^{24a}$, $-OCH_2CO_2H$, 2-(1-morpholino)ethoxy, C_{1-5}alkyl, C_{2-4}alkenyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkylmethyl, C_{2-6}alkoxyalkyl, aryl substituted with 0-2 R^{24}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O;

wherein at least one of A^1, A^2, A^3, A^4, A^5, A^6, A^7, A^8 or R^{23} is a bond to L_n or Q;

R^{24}, R^{24a}, and R^{25} are independently selected at each occurrence from the group: a bond to L_n, a bond to Q, H, C_{1-6}alkyl, phenyl, benzyl, C_{1-6}alkoxy, halide, nitro, cyano, and trifluoromethyl; and

R^{26} is a co-ordinate bond to a metal or a hydrazine protecting group.

137. ***(new)*** A method according to claim 136, wherein:

R is OH;

R^1 is independently selected at each occurrence from the group: H, OH, C_{1-3}alkyl, C_{2-3}alkenyl, C_{2-3}alkynyl, and heterocycle-S-CH_2-;

R^2 is independently C_{1-6}alkyl;

X is C=O;

R^4 is independently selected at each occurrence from the group: C_{1-6}alkyl, phenyl, and benzyl;

R^8 is OH;

R^9 and $R^{9'}$ are independently H, C_{1-6}alkyl optionally substituted with a bond to L_n or a bond to K, or are taken together with the carbon atom to which R^9 and $R^{9'}$ are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-1 heteroatoms selected from O, N, SO_2 and S, said ring system optionally substituted with a bond to L_n or a bond to K;

R^{10} and R^{11} are independently H, or C_{1-6}alkyl optionally substituted with a bond to L_n or a bond to K, or are taken together with the nitrogen atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing, in addition to the nitrogen atom to which R^{10} and R^{11} are attached, 0-1 heteroatoms selected from O, N, SO_2 and S, said ring system optionally substituted with 0-3 R^{27}, a bond to L_n or a bond to K;

or alternatively,

R^9 and R^{10} are taken together with the carbon atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing, in addition to the nitrogen atom to which R^{10} is attached, 0-1 heteroatoms selected

from O, N, SO_2, and S, said ring system optionally substituted with a bond to L_n or a bond to K;

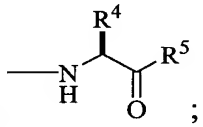
R^{12} is independently C_{1-6}alkyl.

138. ***(new)*** A method according to claim 136, wherein:

R is –OH;

R^2 is C_{1-6}alkyl;

X is C=O;

R^3 is  ;

R^1 and R^4 are taken together to form a bridging group of formula $-(CH_2)_3$-O-phenyl-CH_2-; and

R^5 is NH(C_{1-6}alkyl), substituted with a bond to L_n or a bond to K.

139. ***(new)*** A method according to claim 136, wherein:

R is –OH;

R^9 is C_1alkyl substituted with a bond to L_n; and

R^{10} and R^{11} taken together with the nitrogen atom to which they are attached form a 5 atom saturated ring system, said ring system substituted with 0-3 R^{27}.

140. ***(new)*** A method according to claim 136, wherein:

R is –OH;

R^1 and R^2 taken together with the nitrogen and carbon atom through which they are attached form a saturated ring system containing 5-7 carbon atoms substituted with one or more substituents selected from the group consisting of: a bond to L_n, a bond to K, and $-C(=O)-NR^{29}R^{30}$;

R^{29} and R^{30} taken together with the nitrogen atom through which they are attached form a saturated ring system containing 5-7 carbon atoms substituted with R^{31}; and

R^{31} is a benzyloxy group substituted with C_{1-4}alkyl.

141. ***(new)*** A method according to claim 136, wherein:

W^1 and W^2 are independently selected at each occurrence from the group: O, NH, NHC(=O), C(=O)NH, $NR^{15}C(=O)$, $C(=O)NR^{15}$, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO_2, $-(CH_2CH_2O)_{76-84}-$, $(OCH_2CH_2)_s$, $(CH_2CH_2O)_{s'}$, $(OCH_2CH_2CH_2)_{s''}$, $(CH_2CH_2CH_2O)_t$, and $(aa)_{t'}$;

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-1 R^{16}, C_{3-10}cycloalkyl substituted with 0-1 R^{16}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R^{16};

R^{13}, R^{13a}, R^{14}, R^{14a}, and R^{15} are independently selected at each occurrence from the group: H, =O, COOH, SO_3H, C_{1-5}alkyl substituted with 0-1 R^{16}, aryl substituted with 0-1 R^{16}, benzyl substituted with 0-1 R^{16}, and C_{1-5}alkoxy substituted with 0-1 R^{16}, $NHC(=O)R^{17}$, $C(=O)NHR^{17}$, $NHC(=O)NHR^{17}$, NHR^{17}, R^{17}, and a bond to K;

k is 0 or 1;

s is selected from 0, 1, 2, 3, 4, and 5;

s' is selected from 0, 1, 2, 3, 4, and 5;

s" is selected from 0, 1, 2, 3, 4, and 5; and

t is selected from 0, 1, 2, 3, 4, and 5.

142. ***(new)*** A method according to claim 136, wherein:

W^1 is $C(=O)NR^{15}$;

h is 1;

g is 3;

R^{13} and R^{14} are independently H;

x is 1;

k is 0;

g' is 0;

h' is 1;

W^2 is NH; and

x' is 1.

143. ***(new)*** A method according to claim 136, wherein:

x is 0;

k is 1;

Z is aryl substituted with 0-3 R^{16};

g' is 1;

W^2 is NH;

R^{13a} and R^{14a} are independently H;

h' is 1; and

x' is 1.

144. ***(new)*** A method according to claim 136, wherein:

W^1 is C(=O)NR^{15};

h is 1;

g is 2;

R^{13} and R^{14} are independently H;

x is 1;

k is 0;

g' is 1;

R^{13a} and R^{14a} are independently H; or $C_{1\text{-}5}$alkyl substituted with 0-3 R^{16};

R^{16} is SO_3H;

W^2 is NHC(=O) or NH;

h' is 1; and

x' is 2.

145. ***(new)*** A method according to claim 136, wherein:

W^1 is C(=O)NH;

h is 1;

g is 3;

R^{13} and R^{14} are independently H;

k is 0;

g' is 0;

x is 1;

W^2 is -NH(C=O)- or $-(OCH_2CH_2)_{76\text{-}84}$-;

h' is 2; and

x' is 1.

146. ***(new)*** A method according to claim 136, wherein:

x is 0;

k is 0;

g' is 3;

h' is 1;

W^2 is NH; and

x' is 1.

147. ***(new)*** A method according to claim 136, wherein

x is 0;

Z is aryl substituted with 0-3 R^{16};

k is 1;

g' is 1;

$R^{13a}R^{14a}$ are independently H;

W^2 is NHC(=O) or $-(OCH_2CH_2)_{76\text{-}84}$-; and

x' is 1.

148. ***(new)*** A method according to claim 136, wherein:

W^1 is C=O;

g is 2;

R^{13} and R^{14} are independently H;

k is 0;

g' is 0;

h' is 1;

W^2 is NH; and

x' is 1.

149. ***(new)*** A method according to claim 136, wherein:

h' is 1;

W^2 is NH; and

x' is 1.

150. ***(new)*** A method according to claim 136, wherein:

x is 0;

Z is aryl substituted with 0-3 R^{16};

k is 1;

g' is 1;

$R^{13a}R^{14a}$ are independently H;

W^2 is NHC(=O) or $-(OCH_2CH_2)_{76\text{-}84}$-; and

x' is 1.

151. ***(new)*** A method according to claim 136, wherein:

W^1 is C=O;

g is 2;

R^{13} and R^{14} are independently H;

k is 0;

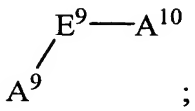
g' is 0;

h' is 1;

W^2 is NH; and

x' is 1.

152. ***(new)*** A method according to claim 136, wherein K is a lipid or a compound of the formula:



;

wherein:

A^9 is OR^{32};

A^{10} is OR^{32};

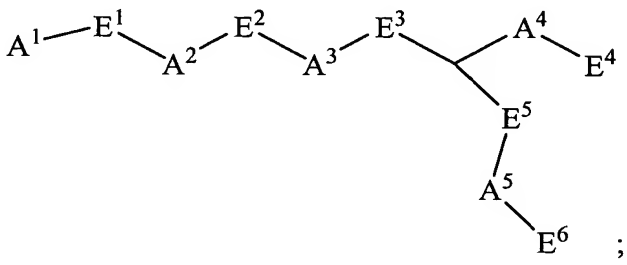
R^{32} is $C(=O)C_{1\text{-}15}$alkyl;

E^9 is $C_{1\text{-}4}$alkylene substituted with 1-3 R^{33};

R^{33} is independently selected at each occurrence from the group: R^{35}, $-PO_3H\text{-}R^{35}$, =O, $-CO_2R^{34}$, $-C(=O)R^{34}$, $-CH_2OR^{34}$, $-OR^{34}$, and $C_{1\text{-}5}$alkyl; and

R^{34} is independently selected at each occurrence from the group: R^{35}, H, $C_{1\text{-}6}$alkyl, phenyl, and benzyl.

153. ***(new)*** A method according to claim 136, wherein K is a compound of the formula:



;

wherein:

A^1 is a bond to L_n;

E^1 is C_1 alkyl substituted by R^{23};

A^2 is NH;

E^2 is C_2alkyl substituted with 0-1R^{23};

A^3 is –O-P(O)(R^{21})-O-;

E^3 is C_1alkyl;

A^4 and A^5 are each –O-;

E^4 and E^6 are each independently C_{1-16}alkyl substituted with 0-1R^{23};

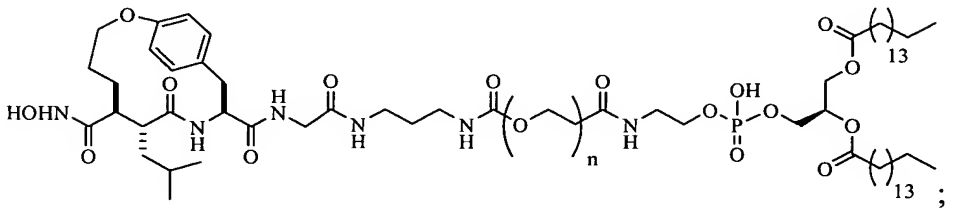
E^5 is C_1 alkyl;

A^5 is –O-;

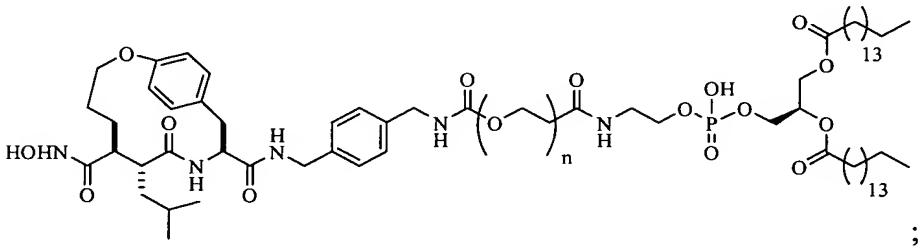
R^{21} is –OH; and

R^{23} is =O.

154. ***(new)*** A method according to claim 136, wherein the compound is:



;



; or

pharmaceutically acceptable salt thereof.

155. ***(new)*** A method according to claim 136, wherein the echogenic gas is a perfluorocarbon gas or sulfur hexafluoride.

156. ***(new)*** A method according to claim 155, wherein said perfluorocarbon gas is selected from the group consisting of perfluoromethane, perfluoroethane,

perfluoropropane, perfluorobutane, perfluorocyclobutane, perfluoropentane, and perfluorohexane.